

Writing your NIH Significance section

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Remember, there is no such thing as “background”. There is not a lot of space in an NIH grant to provide general background information about your research. It is important that you make the most of every word on the page to drive home the rationale, preliminary data, and impact of your work.

In general, I tend to think about my Significance and Preliminary data as woven together in a “call and response” format. This follows the “WHY then WHAT” approach I take for scientific writing. One paragraph first sentence highlights a need or gap, and the next shows preliminary data of how we will fill that gap. **This means the gaps need to be directly addressed by the studies proposed.** If you talk about a lot of gaps without saying how you address them, then the reviewer will need to remember you said it when it comes up later, and the connection may not be very obvious. Also, this makes it very difficult for a reviewer to write a critique.

The first sentence of each significance paragraph should be explicit in stating a gap or how you will address that gap, often with preliminary data. To identify gap statements, take a look at these things that the NIH wants to know in the significance section. These statements are highly useful for reviewers to find the information they need to write a critique and to advocate for your grant.

Significance statement guidelines from the NIH sf424

- Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.

First sentence of each paragraph should provide a coherent, self-standing sentence that answers each of these questions. This will help your reviewer write a review and advocate for your grant. Do not start the sentences with statement of general fact that are not connected to actions your will specifically take in the proposal.

- Generate the thesis statements first (see examples on next page)
- You can then go and make you general factual statement and begin your argument.
- Each sentence in the paragraph should support it.
- You should refer to your aims in the significance section because this is about the significance of your proposal, and not general background significance for your population/disease/questions.
- Check if these statements would work well for the reviewer to put in his bullet point NIH review under strengths of the “Approach”, “Significance”, “Investigator”, “Innovation”, and “Environment”

Preliminary data: These are typically woven into later significant paragraphs, showing you are qualified and ready to address the stated advances. You can also make explicit sections such as “Preliminary data for Aim 1”, etc.

- Generate one sentence for each figure or figure panel that developed a logical argument for what you propose to do in the approach.

In some cases, it may be more appropriate to put your preliminary data in the approach with each specific study you propose. Remember that the main point of the grant is to have reviewers evaluate what you propose to do, so as long as they don't have to wait for pages to find out what that is.

Here are examples of the first sentences of each paragraph of a significance section.

Basically, I want to help the reviewer understand the rationale and evidence without having to search through the paragraphs. I also want to make sure they do not have to infer my points based on a sequence of logic (which is the structure of each associated paragraph). I also want to provide quotes they can use in their review.

I bold the first sentence of each paragraph so the reviewer can quickly see the structure of my argument. content of each paragraph should provide support for the assertion in the first sentence. The "background" statement you may typically use to start a paragraph can be in the second paragraph. Once you make the main assertion, you can rewind back to the beginning and build a train a logic. Typically a paragraph will end with an explicit reference to one or more of your aims; it tells the reviewer exactly what you will do to fill the gap that you have identified.

Example significance first and last sentences:

(First paragraph – "call") **Balance impairments are prevalent in individuals with Parkinson's disease (PD)^{21,22}, but the underlying neural mechanisms are poorly understood, limiting progress for treatment.**

...

In our **Aims**, we seek to gain an individualized understanding of the neural circuit pathophysiology underlying non-motor and motor symptoms of PD to enable new personalized intervention strategies to prevent the negative impact of PD on mobility and quality of life.

(Second paragraph – "response") **We will identify individual differences in brain-behavior relationships based on our prior work demonstrating associations between non-motor symptoms with mobility impairments and fall history in PD.**

...

Our work motivates neurophysiological investigations to understand perceptual- and cognitive-motor interactions impairing balance in PD.

Example of call and response paragraph format:

(call) **Abnormal beta oscillations (13-30 Hz) in cortical regions are associated with PD pathophysiology and motor symptoms, but their role in balance and falls is not understood.**

...

Cortical beta oscillations may also be transient in PD and associated with rigidity⁹⁷, but

their role in balance impairments is unknown.

(response) **Preliminary data for Aim 1 suggest that whole-body perceptual function during balance recovery is impaired by increased cortical beta power in PD.**

...

In Aim 1, we will test whether higher pre-perturbation SMA beta power is associated with lower perception and balance in PD (Fig. 4H).

Example last paragraph first sentence:

(last paragraph) **We will leverage the diverse expertise of our research team to ensure project success, broad dissemination, and translational applications to improve treatments for balance disorders in PD.**

How to check your own writing. Once you write your significance draft, you can follow a few rules to try to make sure you organize the information in a way that follows the principles above. Typically there will be a reorganization, so each sentence or point should stand alone so you can move it around.

- 1) **Find the main idea of each paragraph** that you want the reader to remember and make a first sentence with it. For many of us, this is may be the last sentence of the paragraph, which you came to after working through all the evidence you presented in the paragraph. Sometimes its buried in the middle of the paragraph. This is great work: circle that sentence. Now rewrite your hard-fought conclusion and present it to the reviewers at the outset of the paragraph so that they will want to read the paragraph. I call this “upside-down writing”.
- 2) **Make sure you have a single point or logical argument in each paragraph.** If you see there are a couple ideas, maybe you need to make two paragraphs, or expand the one topic sentence. If you see similar ideas across multiple paragraphs, you can work on consolidating the ideas so you can make each point once, and in a convincing way.
- 3) **Read only the first sentences of your paragraphs and see if they make a complete and logical outline of the motivation for your grant.** These first sentences are guideposts for the reviewer and also help them skim over the proposal at the time they have to present it during study section. Make sure these are great soundbites to help them remember and write about your proposal.
- 4) **Now that you have the first topic sentences, fill in the content of each paragraph.** First, just take the sentences you have and put them under the correct paragraph. I like to use bullet points so that things can be moved around easily. You want to make sure you have a bin to put in each piece of evidence, whether from the literature or from your published or preliminary data. Once you have all the information you can put them in a logical order and end with what you will do about it in your grant.
- 5) **Rigorously check that each sentence of each paragraph supports the first sentence.** Go through and make sure that the there is no surprising content that was not mentioned in the first sentence. If so, you need to reformulate your first sentence

or make a new paragraph. Only content that helps support your first, thesis statement should be included. Think about it like a proof.

Here is what I wrote about topic sentences in a document “writing a paper is like writing a proof”, available on my Unsolicited Advice blog:

<https://scholarblogs.emory.edu/neuromechanicslab/2024/03/15/writing-a-paper/>

• **Once you have your paragraph topics make sure you stay on topic.** The first sentence of the paragraph should tell the whole story, and the body of the paragraph should provide supporting material for that topic. Think of the first sentence as the title, or the thesis statement you wish to prove, just as in a mathematical proof. Often these statements will end up at the end of a paragraph you write during a stream of consciousness dump that helps you understand what arguments you want to make. I call this up-side down writing. Once you find these gems, reformulate them as the take-home messages that you put at the beginning of the paragraph. Then the next sentence can start from the original paragraph beginning to build the argument. A great skill to learn is to skim through your written first draft text and circle the most salient sentences that encapsulate the message in each paragraph then move it to the beginning and edit your paragraph to suit. I call this “upside-down” writing. Once you are a ninja, you can start to write these sentences when you begin.

- For example: in the first draft of this paragraph the main point is in the last sentence:

Due to experimental limitations, three metrics A, B, and C cannot always be directly compared. However, there are certain experiments in which A and B can be compared and shown to be equivalent. Computational methods further enable B and C to be compared. Through a combination of experimental and computational approaches, and with appropriate control, it is possible to conclude that A and C are equivalent. *Therefore, the transitive property is an important principle for showing equivalence of two metrics that cannot be directly compared experimentally or computationally.*

- Simply moving the last sentence to the beginning gives the reader some context and a target to evaluate whether each subsequent sentence is supporting the take-home message:

The transitive property is an important principle for showing equivalence of two metrics that cannot be directly compared experimentally or computationally. Due to experimental limitations, three metrics A, B, and C cannot always be directly compared. However, there are certain experiments in which A and B can be compared and shown to be equivalent. Computational methods further enable B and C to be compared. Through a combination of experimental and computational approaches, and with appropriate control, it is possible to conclude that A and C are equivalent.

- Think of this sentence as the title of your power point slide, or the main thing you want readers to remember. This makes the text easier to read so that the reader can look at the first sentence of each paragraph and skip it if they agree with the thesis. This makes it especially important that you do not add additional ideas into the paragraph. If there are extra ideas in the paragraph, you either need to change the topic sentence, or make a new paragraph.